

## **Draft Investigator Responsibilities Requirement for SAS consideration**

Secretary of Health and Human Services  
200 Independence Avenue, S.W.  
Washington, D.C. 20201

Dear Secretary Sebelius:

In accordance with the provisions of the charter for the Secretary's Advisory Committee on Human Research Protections (SACHRP), I respectfully submit for your consideration a recommendation relative to Department of Health and Human Services Regulation for the Protection of Human Subjects as codified in 45 CFR Part 46. This letter represents the xxx in a series of recommendations from SACHRP.

The HHS 45 CFR 46 Regulation for the Protection of Human Subjects in Research, unlike FDA regulations, does not directly address the roles and responsibilities of investigators involved in human subjects research. Investigators are the individuals that have direct contact with human research subjects and are in the best position to protect participants. While IRBs serve a critical function, they are removed from the day-to-day research activities and thus their ability to monitor research activities is limited. The NIH and FDA have partially addressed the need for enhanced focus on investigator responsibilities through training in grant requirements, guidance and product approval regulations; however, these regulations address only clinical and biomedical investigators.

SACHRP proposes the addition to 45 CFR 46 of three sections that would cover, at a minimum: (1) responsibilities of investigators; (2) qualification standards for investigators (e.g., training); and (3) investigator documentation/records.

New regulations to ensure investigator accountability would codify the current ethical expectations for investigators who conduct human subjects research. Regulations addressing investigator responsibility should emphasize the critical role of the investigator and hold the investigator directly accountable for his/her actions. As part of the FWA requirements, institutions are responsible for ensuring that the regulations are effectively applied. The oversight authority (45 CFR Part 46.103(a)) is already in place: "each institution engaged in research ... shall provide written assurance ... that it will comply with the requirements set forth in this policy."

Adding investigator responsibilities to the HHS regulations would harmonize HHS regulations with those of the FDA and international standards, uniting the regulatory expectations. Models for delineating investigator responsibilities can be found in the drug and device regulations of the FDA (i.e., Subpart D, 21 CFR Part 312 and Subpart E, 21 CFR Part 812) and in internationally accepted guidelines such as the ICH standards (Good Clinical Practice E-6, Section 4) and the CIOMS International Ethical Guidelines For Biomedical Research.

Therefore, SACHRP recommends the following language for inclusion in 45 CFR 46:

*§46.104 Responsibilities of Investigators.*

- (a) *Investigators are responsible for ensuring that research is conducted according to:*
  - (1) *sound research design and scientific methods;*
  - (2) *the terms of the grant, contract and/or signed funding agreements, that are applicable to the investigator;*
  - (3) *the IRB approved study plan (protocol);*
  - (4) *applicable laws and regulations including those for protecting the rights, safety, and welfare of human subjects.*
- (b) *Unless exempt from review, investigators are responsible for obtaining initial IRB approval, prior approval for any modifications to the research and, as required, continuing review of the research.*
- (c) *Investigators are responsible for providing the IRB with sufficient information and materials to make the required determinations in §46.111.*
- (d) *Unless waived by the IRB, investigators are responsible for ensuring that informed consent is obtained in accordance with §46.116. Unless waived by the IRB, investigators are responsible for obtaining signed consent to the extent required by §46.117.*
- (e) *Investigators are responsible for providing a copy of the informed consent to each subject, unless the requirement of a written consent document is not part of the IRB approved protocol.*
- (f) *When vulnerable populations are involved in research, investigators are responsible for complying with any required additional safeguards.*
- (g) *Investigators are required to permit and facilitate monitoring and auditing, at reasonable times, by the IRB of record, funding agencies, sponsors, the Secretary, and other federal and state regulatory agencies, as appropriate.*
- (h) *In compliance with §46.103(b)(5) of this subpart, investigators shall ensure prompt reporting to the IRB of any noncompliance with the approved protocol or requirements of the IRB, and unanticipated problems involving risks to subjects or others.*
- (i) *Investigators are responsible for personally conducting or supervising the research.*
- (j) *Investigators are responsible for complying with regulatory and institutional requirements including those relating to financial interests that are relevant to the research*

*§46.105 Qualification Standards for Investigators.*

- (a) *Investigators must be sufficiently qualified by education, training, and experience that is appropriate to their role in the research to assume responsibility for the proper conduct of human subjects research.*
- (b) *Investigators should have sufficient time and resources to properly conduct or supervise the research for which they are responsible.*

*§46.106 Investigator Records, Reports and Documentation.*

- (a) *Investigators are responsible for the safe and secure storage of research data (in both paper and electronic formats) and protecting the confidentiality of the data.*
- (b) *Investigators are responsible for the accuracy and completeness of the data recorded and reported in research and in publications about the research.*
- (c) *Investigators must maintain records appropriate to the research (e.g., the study plan, consent forms, and correspondence from the IRB) and permit inspection of the research records in accordance with §46.104(f).*

- (d) Investigators must maintain records for at least three years after the research ends or for the length of time specified in applicable regulations or applicable institutional or sponsor requirements, whichever is longer, and should take measures to prevent accidental or premature destruction of these documents.*
- (e) Investigators must submit written reports to the IRB as requested/required by the IRB.*